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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/694,475
Filing Date: October 27, 2003
Appellant(s): TEREBA ET AL.

Jill A. Fahrlander
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 7/17/2009 appealing from the Office action mailed 11/18/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed. The 2/17/2009 notice of appeal was filed after the non-final office action mailed 11/18/2008. Applicant's amendment filed therewith was entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct.

The changes are as follows:

Claims 44-54,58,60-70,72-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melzak et al (1996 J. Colloid and Interface Science 181:635-644) in view of Kleiber et al (WO 96/41811 – IDS entry 1/8/2007) and further in view of Ryder et al (US Patent 5639599).

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Melzak, K.A. et al "Driving Forces for DNA Adsorption to Silica in Perchlorate Solutions" J. Colloid and Interface Science vol 181, no. 635, pp 635-644

WO96/41811	**Kleiber et al**	12-1996
5,639,599	**Ryder et al**	6-1997

PUC18 nucleotide sequence downloaded from http://seq.yeastgenome.org/vectordb/vector_descrip/COMPLETE/PUC18.SEQ.html - printed 11/13/2008 (IFW scanning date 11/18/2008).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 USC § 102

Claims 44,45,50,53,65-66,67,82 are rejected under 35 U.S.C. 102(b) as being anticipated by **Melzak et al** (1996 J. Colloid and Interface Science 181:635-644) as

evidenced by the PUC18 nucleotide sequence available at http://seq.yeastgenome.org/

The claimed subject matter per claim 44 is drawn to a method for isolating a defined and consistent amount of DNA from multiple samples comprising:

(a) selecting a defined amount of DNA to be isolated from the samples;

(b) choosing a discrete amount of a silica-containing solid support necessary to isolate the defined amount of DNA from each sample;

(c) contacting each sample with the discrete amount of the silica-containing solid support, each sample comprising DNA in excess of the binding capacity of the discrete amount of silica-containing solid support, under conditions that allow reversible binding of the defined amount of DNA to the solid support; and

(d) separating each sample from the support to isolate a defined and consistent amount of DNA from each sample.

Claims 45,50,53,65, 66, 67 and 82 represent variations thereof.

Melzak et al teach, throughout the document and especially the title and abstract, a study of the dominant driving forces involved in DNA adsorption to silica in perchlorate solutions.

Melzak et al teach in figure 3b, a DNA titration of silica which shows closed circle data points (i.e. multiple pUC18 samples) forming a saturation curve. Said saturation occurs at and above approximately 4 ug/mL DNA.

On p 637, fourth paragraph, Melzak et al teach measuring said silica surface area as 5.6 m^2/g, by BET adsorption, reading on claims 44b and 66b. Said saturation of 380 ug DNA per m^2 on said silica per figure 3b of Melzak et al means said silica provides 2090 ug DNA (5.6 x 380) bound per g silica. On p 638 under 'DNA adsorption measurements' Melzak et al teach 2.8 to 3.1 mg clean dry silica was used for the

experiments, further reading on claims 44b and 66b. In accordance with the open circles in figure 3b of Melzak et al, each of said pUC18 DNA samples are eluted completely (i.e. quantitatively reversibly desorbed), therein each of said closed circle data points represents selecting a defined amount of DNA to be isolated, as set forth in claim 44a and 66a. Past said saturation point, the DNA samples are introduced to the silica in excess of the silica binding capacity, reading on claims 44c and 66c and said quantitative reversible desorption of the full capacity of the silica mentioned above reads on claims 44d, 45, and, absent evidence to the contrary, said eluted DNA may be used in a molecular biology procedure, as set forth in claim 66d. As would be expected for quantitative desorption, the variability of the eluted DNA past the saturation point appears minimal and in the range of claim 82.

Said perchlorate is taken as the chaotropic salt of claim 50. The conditions shown in the legend to figure 3 of Melzak et al indicate said perchlorate is 6 molar, reading on claim 65.

Said pUC18 reads on the plasmid DNA of claim 53 and has a known sequence, available at

http://seq.yeastgenome.org/vectordb/vector_descrip/COMPLETE/PUC18.SEQ.html (print-out IFW date 11/18/2008), which includes short tandem repeats, reading on claim 67.

35 USC § 103

Claims 44,45,50,53,65-66,67,82 and 46-49,51-52,54,58,60-64,68,77-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Melzak et al** (1996 J. Colloid and Interface Science 181:635-644) in view of **Kleiber et al** (WO 96/41811 – IDS entry 1/8/2007).

Melzak et al is relied on as above.

Melzak et al do not teach: magnetic particles, such as set forth in claims 46-49; guanidine thiocyanate (claim 51); genomic DNA (claim 52); further analysis (claim 54); forensic samples (claim 58); heating samples from 60 degrees to 100 degrees (claim 60); sequencing (claim 61); washing with an alcohol and salt (claims 62-63); elution with water (claim 64); Combined DNA Index System Loci (claim 68); DNA amplification (claim 77);sequencing (claim 78); hybridization (claim 79); elution in a discrete volume such that the eluted DNA is from about 0.5 to about 5.0 ng/ul (claims 80-81).

Kleiber et al teach, throughout the document and especially the abstract porous and poreless boro/aluminio/zirconio-silicate magnetic particles useful for DNA isolation. Kleiber et al teach in figure 2 and example 3, separating DNA from said magnetic particles to isolate a defined amount of DNA from each type of particle. For instance, on p 19 first paragraph, Kleiber et al indicate said DNA was eluted from magnetic particle with 3 x 200 microliters, reading on claim 80, and sample GMP/2 on the table on p 21 indicates an ultimate yield of 1.7 ug = 2.8 ng/ul (1.7/600*1000), in the range of claim 81.

Said porous and poreless magnetic particles of Kleiber et al are taken as the siliceous-oxide magnetic particles (elected species) of claims 46, 47, 48 and 49.

Kleiber et al teach chaotropic salts including guanidine thiocyanate on p 9, second paragraph, line 14, reading on claims 50 and 51.

Kleiber et al teach in example 3, the use of blood as a genomic DNA sample, reading on claim 52 (elected species). Said blood is subsequently analyzed in example 3 of Kleiber et al, as set forth in claim 54.

Said blood is taken as type of forensic sample, such as set forth in claim 58 (elected species).

Said blood inherently comprises Combined DNA Index System Loci, as set forth in claim 68.

Said blood is contacted with 6 Molar guanidine HCl, a chaotropic salt at 70 degrees C on p 18, according to Kleiber et al in the second paragraph under Nucleic Acid Isolation, in the range of claims 60 and 65.

Kleiber et al teach on p 19, line 4 washing of the magnetic particles with ethanol/water, reading on claims 62 and 63.

Kleiber et al teach elution with water in the second paragraph on p 11, last line, therein reading on claim 64.

Kleiber et al teach the magnetic particles may be used in concert with molecular biology procedures including amplification, sequencing and hybridization on p 12 first full paragraph, reading on claims 61, 77, 78 and 79.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to apply the procedure of Melzak et al for discerning the dominant driving forces involved in DNA-silica interactions toward the

porous and poreless boro/aluminio/zirconio-silicate magnetic particles according to Kleiber et al.

One of ordinary skill in the art would have been motivated to apply the procedure of Melzak et al for discerning the dominant driving forces involved in DNA adsorption toward the porous and poreless boro/aluminio/zirconio-silicate magnetic particles according to Kleiber et al because a better understanding of DNA-SiO_x interactions would speed development of new tools for DNA diagnostics, such as micromachines, which represents a critical area of research for international competitiveness, as noted by Melzak et al in the second paragraph on p 635.

One of ordinary skill in the art would have had a reasonable expectation of success in applying the procedure for measuring the dominant driving forces involved in DNA-silica interactions described by Melzak et al toward the porous and poreless boro/aluminio/zirconio-silicate magnetic particles according to Kleiber et al because both references concern silica adsorption and desorption of DNA. Thus the magnetic particles of Kleiber et al lie well within the scope of material suitable for analysis in the manner of Melzak et al.

Claims 69-70,72-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Melzak et al** (1996 J. Colloid and Interface Science 181:635-644) in view of **Kleiber et al** (WO 96/41811 – IDS entry 1/8/2007) as applied to claims 44,45,50,53,65-66,67,82 and 46-49,51-52,54,58,60-64,68,77-81 above, and further in view of **Ryder et al** (US Patent 5639599).

Melzak et al in view of Kleiber et al is relied on as above.

Melzak et al in view of Kleiber et al do not teach a kit, as set forth in claims 69-70, 72-76.

Ryder et al teach, throughout the document and especially the abstract, and column 1, lines 14-16, 37-40 kits containing ferric iron complexing agents for nucleic acid isolation.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to include the reagents used by Melzak et al in view of Kleiber et al with the kit such as described by Ryder et al.

One of ordinary skill in the art would have been motivated to include the reagents used by Melzak et al in view of Kleiber et al with the kit such as described by Ryder et al because Ferric ions (Fe^{+++}) interfere with downstream applications, such as amplification, as noted by Ryder et al in column 2 lines 15-16.

One of ordinary skill in the art would have had a reasonable expectation of success in utilizing the iron complexing reagent kit in concert with the reagents used by Melzak et al in view of Kleiber et al because Ryder et al envisions an embodiment including silica in patent claim 21. Furthermore, all three references concern nucleic acid isolation, thus the kit including iron complexing agents lie well within the scope of technology according to Melzak et al in view of Kleiber et al.

(10) Response to Argument

On p 11 of the appeal brief entered 7/17/2009, appellant notes seven references have been overcome over the course of prosecution, including Smith et al. It is noted however, since the current rejections are over Melzak et al and combinations thereof, (i.e. not Smith et al) it is not clear what relevance appellant's arguments concern as to the current rejection.

Similarly, the Bitner declaration, appended to the end of the appeal brief, addresses references such as Huber et al and Volgelstein et al, which are not currently of concern either.

The Examiner's Answer addresses the appeal brief arguments germane to the rejections at hand.

Anticipation Argument

In the appeal brief filed 7/17/2009, appellant argues (i) not all elements are taught; (ii) the aim of Melzak et al differs from the present claimed invention. Specifically in the paragraph bridging pages 11 - 12, appellant argues Melzak does not anticipate the claims. The rejection, however, is for obviousness, not anticipation. Therefore the arguments have been considered as to obviousness but are unpersuasive in view of the following discussion.

Appellant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

(i) Specifically, on p 12 first full paragraph, appellant argues Melzak et al do not teach "(a) selecting a defined amount of DNA to be isolated from the samples and (b) choosing a discrete amount of a silica-containing solid support necessary to isolate the defined amount of DNA from each sample."

In this vein, the following is noted. The loading (binding) capacity of a given solid support is of interest in a whole host of techniques, such as chromatography, solid-phase synthesis and solid phase extraction (such as the presently claimed method), because it provides the skilled artisan the maximum amount of adsorbate which will bind to a support.

The binding capacity of a given solid support is measured using a saturation curve, generated by titrating increasing amounts of adsorbate (i.e. multiple samples), such as illustrated in figure 3 of Melzak et al. Please note, as admitted by applicant in section 10 of the attached declaration, Greenspoon & Ban perform a somewhat analogous experiment using serial dilutions of semen DNA. The portion of the curve which is flat represents the saturation point or maximum amount of adsorbate that may be loaded. In Melzak et al figure 3B, this occurs above ca. 4 ug/mL supercoiled DNA (380 ug/m^2 silica).

Loading capacity is more commonly reported in moles adsorbate per gram support or mg adsorbate per gram support and while Melzak et al present their data in terms of ug DNA per square meter, the surface area of the silica is provided on p 637, fourth paragraph as 5.6 m^2/g. Accordingly, the supercoiled DNA loading capacity of the

silica analyzed by Melzak et al is 2090 ug DNA bound per g silica (5.6 m^2/g x 380 ug/m^2 silica).

Since the silica of Melzak et al figure 3B has reached its saturation point past 4 ug/mL supercoiled DNA and provided elution (desorption) occurs quantitatively (100 %) - which Melzak et al illustrate with the open circle data points in figure 3B - the ca. 3 mg (2.8 – 3.1 mg) silica aliquots (see p 638 under 'DNA adsorption measurements') each desorb ca. 6.27 ug DNA (2090 ug DNA/g silica x 3 mg silica x 1g/1000mg). Said 6.27 ug DNA constitutes selecting a defined and consistent amount of DNA to be isolated from the samples as set forth in claims 44a and 66a. Said ca. 3 mg silica constitutes choosing a discrete amount of a silica-containing solid support necessary to isolate the defined amount of DNA from each sample, as set forth in claims 44b and 66b.

(ii) On p 12 second paragraph through the paragraph bridging pp 12-13 of the brief, appellant argues the aim of Melzak et al in figure 3 is to investigate whether DNA superstructure impacts adsorption characteristics rather than isolating a defined and consistent amount of DNA from multiple samples and choosing a discrete amount of silica-containing solid support necessary to isolate the defined amount of DNA from the samples.

Where goal of Melzak et al may differ from the claimed invention, this does not, however, change the fact that each step of the rejected claims are undertaken by Melzak et al: Past the saturation point (DNA in excess of the binding capacity), the elution of supercoiled pUC18 from multiple samples generates a defined amount of DNA based on the loading capacity of the silica.

Obviousness

On p 15 first full paragraph of the appeal brief filed 7/17/2009, in addition to not all elements not being taught, as addressed above, appellant urges secondary considerations support the non-obviousness of claimed invention, as evidenced by the attached Bitner Declaration.

In this vein, appellant notes the claimed invention (DNA IQ™) has received praise in terms of receiving a R&D 100 award (Bitner declaration sections 5 and 16) and cites *Vulcan Engineering Co. v. FATA Aluminum Inc.* 278 F3d 1366; 61 USPQ2d 1545: "Appreciation by contemporaries skilled in the field of the invention is a useful indicator of whether the invention would have been obvious to such persons at the time it was made," thus appellant argues that praise of others constitutes an indicia of non-obviousness.

In this regard, the examiner notes the above quotation taken in context with the Federal Circuit decision concerned commercial success. And, according to MPEP 716.03(b), In *ex parte* proceedings before the Patent and Trademark Office, an applicant must show that the *claimed features were responsible for the commercial success* of an article if the evidence of nonobviousness is to be accorded substantial weight. See *In re Huang*, 100 F.3d 135, 140, 40 USPQ2d 1685, 1690 (Fed. Cir. 1996) Here, it is not clear if the claimed features were responsible for the praise in the form of the R&D 100 award since appellant has not provided the criteria for the earning the award. Not to disparage the award sponsors or the importance of the present application, but accordingly, the R&D 100 award is not accorded substantial weight.

Response to Declaration

On p 15 first full paragraph of the appeal brief filed 7/17/2009 appellant urges secondary considerations with regard to long felt need support the non-obviousness of claimed invention, as evidenced by the attached Bitner Declaration.

In particular, appellant argues the claimed method addresses the long felt need in the industry of isolating a defined and consistent amount of DNA from multiple samples and doing so in a manner that simplifies processing, reduces the amount of sample required and time spent processing.

In so far as considering a long felt need, according to MPEP 716.04, the following three prong test is applied. First, the need must have existed for a long period of time without solution. Second, the long felt need must be established by evidence concerning the failure of others. Third, the invention must, in fact, satisfy the long felt need.

With regard to the first prong, the examiner acknowledges the Bitner declaration, especially section 8 and last page of exhibit E, provides evidence for the need for improving DNA sample throughput has existed for a long period of time without solution. Notably however, with regard to the second prong, the declaration does not address the failure of others. In particular, none of the exhibits address the failure of prior art methods or other systems from other manufactures, etc. In fact, appellant admits in section 6 of the declaration that prior approaches did *not* isolate a defined and consistent amount of DNA from multiple samples but rather focused on maximizing

DNA yield instead. While the Gorman letter and Greenspoon & Ban paper (exhibits B and D) provide some evidence that prior approaches were laborious and time consuming, no evidence is presented that the previous approaches isolated an ill-defined or inconsistent amount of DNA from multiple samples. With regard the third prong of actually satisfying the long felt need of improving DNA sample throughput, it is noted neither the paper by Greenspoon & Ban or the letter from the latter author (exhibits B and E) addresses whether the improved DNA sample throughput is due to the DNA IQ ™ or rather the Beckman Coulter Biomek ® 2000 robotic workstation which would provide improved throughput through automation.

Lastly, in regard to a manner that simplifies processing, reduces the amount of sample required and time spent processing as mentioned on p 15 first paragraph of the appeal brief, in response to appellant's argument that the references fail to show certain features of appellant's invention, it is noted that the features upon which appellant relies (i.e., a manner that simplifies processing, reduces the amount of sample required and time spent processing) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant does not offer further arguments regarding the obviousness rejection over Melzak et al in view of Kleiber et al and further in view of Ryder et al beyond what was set forth with regard to the 35 U.S.C. § 102 rejection over Melzak et al discussed above. To the extent that Appellant is merely repeating their previous argument; the

examiner contends that those issues were adequately addressed in the above sections, which are incorporated in their entireties herein by reference.

Conclusion

The steps undertaken by Melzak et al anticipates the claimed subject matter set forth in independent claims 44 and 66 as well as claims 45,50,53,65,67,82. The remaining dependent claims are constitute obvious variants and appellants arguments regarding commercial success and long felt need as secondary considerations are not persuasive.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Christopher M. Gross/

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